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**REVIEW 1227** 

CONFIDENTIAL

Box F3

"Cigarette nicotine yields and nicotine intake among

Japanese male workers"

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This paper describes a cross sectional study of 246 male smokers of at least 10 cigs/day, conducted in Japan in 1997, which related the machine nicotine yield of the brand smoked to:

- (i) the urinary nicotine metabolite concentration (nicotine, cotinine and trans-3. hydroxycotinine) in mg/g cotinine,
- (ii) the estimated daily nicotine intake (mg),
- (iii) the self-reported daily cigarette consumption and
- (iv) the estimated intake of nicotine (mg) per cigarette smoked.

In the conclusions of the paper it is stated that:

"In this study of Japanese male smokers, actual levels of nicotine intake bore little relation to advertised nicotine yield levels. Our study reinforces the need to warn consumers of inappropriate advertisements of nicotine yields, especially low yield brands" while, in the "what this paper adds" section of the paper, it is stated that:

"Previous studies have found little relation between the advertised nicotine yield of cigarettes and concentrations of nicotine metabolites measured in smokers. However, few studies have included smokers of "ultra low" brands (cigarettes yielding  $\leq 0.1$  mg of nicotine by FTC methods). Data are also sparse in countries outside Britain and the USA. We conclude that, based on the concentrations of urinary biomarkers, the FTC nicotine yields in cigarette smoke were not equivalent to nicotine exposure at any advertised yield level. Moreover, ultra low and low yield cigarettes may not reduce the risk of ill health."

It is certainly true that data relating brand nicotine yield to nicotine intake are sparse in

countries other than the UK and US. Such data are also sparse on smokers of "ultra low" brands – the study compares smokers in four groups of brand nicotine yield: 0 to 0.1, 0.1 to <0.6, 0.6 to <1.0 and ≥1.0 mg/cig. However, the way the rest of this section and also the conclusions section is phrased is seriously unhelpful, projecting politically-correct rather than true scientific conclusions.

The study actually presents two quite interesting and important findings which are given far too little emphasis. The first is the fact, seen in Table 2 on p 58, that self-reported daily cigarette consumption was very similar in the four nicotine yield groups. Now this finding, in a cross-sectional study, does not necessarily demonstrate that switching to a lower nicotine brand does not result in increased consumption – it may be that those who chose to switch were "less addicted" smokers who tended to smoke less before they switched and did increase consumption somewhat. However, it certainly does not provide any basis for the possibility of a substantial increase in amount smoked following a switch to lower nicotine cigarettes, given (inappropriately) so much attention in chapter 4 of the recent NCI Monograph 13 on "Risks associated with smoking cigarettes with low machine-measured yields of tar and nicotine."

The second finding of major interest is that, as also seen in Table 2, there was a clear and significant tendency for urinary nicotine metabolite concentration, daily nicotine intake and estimated nicotine intake per cigarette to decline with reducing machine nicotine yield of the cigarette smoked. Compared to high yield (>1.0 mg/cig) smokers, ultra low yield (0-0.1 mg/cig) smokers had levels for all these three indices of exposure that were less than half as great (e.g. 0.59 vs 1.36 mg for nicotine intake per cigarette). Given that there have been so many (unjustified) claims in the literature (and media) that smokers smoke for a given level of nicotine and that switching to a brand with a reduced machine-yield of nicotine does not involve any actual reduction in exposure, the authors place no emphasis at all on their results, which seem consistent with compensation actually being far from complete (though inferences are limited from a cross-sectional study).

In fact, the results seem absolutely consistent with my own interpretation of the literature, expressed on various occasions, that compensation as regards amount smoked is quite small at most and that compensation as regards the method of smoking the cigarette, though substantial,

is far from being complete. It is clearly true that nicotine intake per cigarette smoked does not directly correspond to the machine nicotine yield, but this has been known for decades. Emphasising, as the authors do, this lack of correspondence, is unhelpful; the important thing to note is that smokers of lower yield cigarettes do have lower intakes, consistent with the epidemiological evidence<sup>2</sup> of their lower risk of lung cancer.

Some other less important points to note on the paper are:

- (i) Table 1 includes results relating machine nicotine yield to various characteristics of smokers and smoking behaviours. I suspect that the chisquared test results given are inappropriate as they do not specifically test for a trend between the machine nicotine yield and inhalation, time to first cigarette in the morning, quit attempts in the past and "stage of change" (which is unexplained and means nothing to me). I suspect that the tendency for low-yield smokers to inhale less, to be more likely to attempt quitting and to have the first cigarette in the morning later are all more significant than reported. These findings are all consistent with those choosing to smoke lower yield products being less likely to be "addicted" smokers, which is not unexpected.
- (ii) Figure 1 shows a scatterplot relating urinary nicotine metabolite concentrations to cigarette nicotine yield. The authors comment that the correlation (r = 0.23, p<0.001), though significant, is small. Given the large variation between subjects in nicotine metabolite concentrations for a given nicotine yield, it is not at all clear that the correlation is so small. Even if, within any individual, nicotine intake were directly related to nicotine yield by a straight line going through the origin, one would not expect that the correlation, measured in this way, would be large. It is a common and false inference to argue that brand nicotine is unimportant just because correlations are not high.

P N Lee 17.5.2002



## References

- 1. United States Department of Health and Human Services USDHHS. Monograph 13. Risks associated with smoking cigarettes with low machine-measured yields of tar and nicotine. US Department of Health and Human Services; 2001. (Smoking and Tobacco Control.)
- 2. Lee PN. Lung cancer and type of cigarette smoked. Inhal Toxicol 2001;13:951-76.